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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,351	10/18/2001	Aleem Gangjee	049450-00170	6712

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EXAMINER
BERCH, MARK L

ART UNIT	PAPER NUMBER
1624	6

DATE MAILED: 07/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/982,351	GANGJEE, ALEEM	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *12-14,21 and 23-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15-20,22 and 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 21, 23-28, drawn to furopyrimidines, classified in class 544, subclass 278.

II. Claims 22, 29-34, drawn to pyrrolopyrimidines, classified in class 544, subclass 280.

III. Claim (none), drawn to other, classified in class 544 and 540, subclass various.

Claims 1, 15-20 link inventions I and II and III.

Claims 2-11 link inventions II and III.

Claims 12-14 link inventions I and III.

The inventions are distinct, each from the other because of the following reasons:

Groups I and II are distinct as seen by the nature of the heterocycle core. Group I has a core with a 5-membered ring containing one oxygen; Group II has only heterocyclic nitrogen. Group III has an assortment of cores. The second ring could be an imidazole (to form a purine), pyridine, thiophene, pyrimidine, pyridazine and assorted 7 membered rings including azepines.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with D. Anderson on 7/1/02 a provisional election was made with traverse to prosecute the invention of Group II , claims 1-11, 15-

20, 22, 29-34. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-14, 21, 23-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-11 and 15-20 are rejected as being drawn to an improper Markush Group. The claims are drawn to multiple inventions for reasons set forth in the above requirement for restriction. This does not constitute an art recognized genus. The claims are examined only to the extent that they read on the elected invention. Cancellation of the non-elected subject matter will overcome the rejection. These claims are examined to the extent that they read on the elected invention.

Specification

The abstract of the disclosure is objected to because it is too general. The structure, with the definitions of L, M and Z is needed. Correction is required. See MPEP § 608.01(b).

Pages 20-25 were not copied correctly and will need to be replaced.

The next to last row in Table 4 is unclear: What exactly is this?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 15-17, 19-20, 22, 29-31, 33, 34 are rejected under 35 U.S.C. 102(a, e) as being anticipated by Norman et al.

See the species at column 78, line 50, column 79, line 10. Assuming that X being H corresponds to a bond, this species corresponds in claim 29 to X = X2 = R1 = H, R3 = aryl for the column 78 species, and X = X2 = H, R3 = aryl, R1 = cyclic heteroaliphatic. Cancer is listed in the abstract, at column 20, line 4 and elsewhere. Many other species anticipate claims 1 and 2.

Claims 1-3, 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Gangjee.

The language of claims 18 and 26 appear e.g. in the abstract, along with cancer.

Claims 1-2, 15-17, 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Traxler '457 or Traxler et al.

See compounds of formula I in '457, used as anti-tumor agents, and the compounds of Table 2 and Table 3 in Traxler et al..

Claims 1-2, 15-17, 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Missbach.

See compounds of formula I, used as anti-tumor agents.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 15-20, 22, 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Language such as page 29 line 3 does not make sense. The formula already specifies that all five be present.
2. The choice of X as H does not make sense, as H cannot carry a substituent. It is assumed that "bond" is intended.
3. The other X choices should be written as divalent radicals, e.g. alkylene, not alkyl.
4. Similarly in claim 3, that should be NH, not NH_2, since the latter is not divalent.
5. The terms "cyclic aliphatic" and "cyclic heteroaliphatic" make no sense. An aliphatic group by its very nature is not cyclic. This phrase is thus a contradiction in terms.
6. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The meanings given on page 8 by applicants are not the usual meaning at all. Alkyl is a group of the formula $-C_nH_{2n+1}$, as is set forth in such sources as Hack's Chemical Dictionary and Hawley's Condensed

Chemical Dictionary, or any textbook of organic chemistry. As such it cannot have rings.

7. The term "heteroaliphatic" is unclear. It could mean a) an aliphatic group attached via a heteroatom b) and aliphatic group which contains a heteroatom somewhere c) a heterocyclic ring attached via an aliphatic group or d) an aliphatic group further substituted by a heterocyclic ring. The problem with a) and b) is that an aliphatic group is already permitted to have a heteroatom, so that the "hetero" part would make no sense. That is, a methoxy group, or a halomethyl group is aliphatic already. That is, "aliphatic" is already embracive of groups which have a heteroatom present.
8. "Prodrug thereof" is indefinite. Determining whether a given derivative definitely is or is not a prodrug involves more than routine experimentation. If the derivative is active, open-ended experimentation may be involved to determine for sure whether the compound is a prodrug or whether it is active in its own right (paragraph 2).
9. Claim 20 does not further limit claim 16, and hence claim 20 is improperly dependent on claim 16. The term "including" does not limit. Likewise claim 34.
10. The material at page 28, lines 9-11 makes no sense. Such groups are already provided fro. Thus, an e.g. alkenyl group which is further substituted by an alkyl group is still an alkenyl group, and thus is already covered. This material adds nothing to the claim.
11. Divalent choices for L and Z are impossible, i.e. CH_2, NH, S and O. These atoms must have either three or 4 bonds attached to them (two ring bonds, a third bond to an X and a 4^{th} depending on whether or not there is a double bond). The divalent choices, however, can only have 2 bonds.

12. The wording of "Receptor Tyrosine Kinase" is not correct. This implies that there is an enzyme with this name, but that is not so. Note the cited reference Receptor Tyrosine Kinases (RTKs) chart from http://www.kinase.com/mammalian/rtks.pdf This shows that there is in fact a entire family with over 20 sub-families, and dozens of specific enzymes. And these are just the human ones; there are mouse isologs, and ones for zebra fish, etc. Moreover, these are not at all equivalent to each other. Thus, the Eph family of receptor protein tyrosine kinases and their ligands, the ephrins, have a role in developmental neurobiology as molecular guides for axons and may be involved in other processes such as cancer, angiogenisis, haematopoiesis, and kidney development. INSR is an insulin receptor, and others are involved in others activities.

Claims 15, 16, 19, 20, 29, 30, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to treating illnesses generally. The term "an illness" appears without limitation, and hence would cover treating any illness of any type. Obviously, such is not enabled, not does the specification state that these compounds are a panacea.

In addition, this appears to be covering the inhibition of RTKs generally. As noted above, these are diverse, and there is no evidence that these compounds are active generally. Applicants' Table 4 is noted, but this tests only 4 RTKs. Moreover, the

compounds generally are not active against even these four. Only one was active against all 4, and only one was active against 3 of the 4.

Claims 17 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim sets forth the treatment of cancer generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ

609. The failure of skilled scientists to achieve a goal --- and there have been massive efforts made to find an agent effective generally against cancer --- is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006.

It is noted that these are RTK antagonists. The references cited by applicants have been reviewed. While control of angiogenisis is a promising research area, the idea that it can be used general is currently without scientific basis; indeed, no such drug has been yet made to work as of the filing date. Moreover, even if the broadest possible success were possible, that still would be of no avail against non-solid tumors e.g. leukemias.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.

Mark L. Berch
Primary Examiner
Art Unit 1624

July 11, 2002